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Do present levels of air pollution outdoors affect respiratory health?

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A sensitive lung function test does not show differences due to air pollution between lifetime residents in a rural area and those in a small industrial town in Connecticut. Also, there is no evidence that higher air pollutant concentrations elsewhere have any marked effects on the lungs. Severe pollution is dangerous and must be avoided, but at present, air pollution control outdoors does not deserve priority as a means of preventing chronic lung diseases.

WE have assessed the impact of urban residence on respiratory health in the population of an industrial US town, in comparison with a rural population which included lifetime dwellers as well as migrants who had previously lived in cities. We determined differences in respiratory health between these populations from (1) the prevalence of common respiratory symptoms, and of bronchitis and asthma, and (2) lung function tests which reflect airway calibre. As air pollution outdoors is one 'urban factor' which may affect the health of people living in cities, we monitored several air pollutants at different sites in both towns.

The urban area had a record of high air pollution (by US standards) in the recent past, but the urban–rural pollution contrast at the time of our study was modest. We therefore also compared our results with data on people living in more severely polluted urban areas, and in other rural areas, so as to expand the pollution contrast.

To assess respiratory health in both towns, we used a questionnaire and a sensitive, standardised lung function test. We studied children and adults of both sexes, and healthy persons as well as those with respiratory symptoms or disease. Our population samples were large and representative of the total population of both areas. In analysing the results, we took into account sex, race, age, body height, body weight, smoking habits, occupation and previous residence. We believe that this is the first report of a study which combines all these features, and that it allows more reliable conclusions concerning urban factors and chronic respiratory disease (other than lung cancer) than do previous studies.

Populations and air pollution

The urban site, Ansonia, Connecticut, is an industrial town where mean annual particulate concentrations were among the highest measured in Connecticut during 1966–72 (88–152 $\mu g\,m^{-3}$; ref. 1); high SO_2 concentrations (by US standards) were probably also common in the past. In 1973, particulate concentrations were lower but still significantly higher than at the contrasting rural site, Lebanon, Connecticut. Lebanon is a sparsely populated town without factories or major highways, away from cities. Outdoor pollutants (Table 1) were monitored in both towns for more than 1 yr, including the period of our population surveys[1,2]. Concentrations of total suspended particulates (TSP, high-volume samplers) and of nitrogen dioxide were significantly higher at the urban sites, as were nitrates and sulphates (data in refs 1, 2). There were no significant differences for sulphur dioxide and ozone.

In two geographically defined areas (the town of Lebanon and the 4th Ward of Ansonia), we attempted to study all residents aged ⩾ 7 yr. Response rates varied from 91–96% among boys and girls (7–14 yr) in both towns to 56% and 80% among 25–64-yr-old adults in Ansonia and Lebanon, respectively. From a private census and interviews of nonresponders[3], we concluded that the responders adequately represent the total populations. There were only 20 black residents of Lebanon; our main analyses are therefore limited to the white residents of Lebanon and Ansonia (Table 2). Of the Lebanon subjects, 41% had previously lived in urban areas, possible selection factors made it important to consider these subjects separately from lifetime rural (LR) dwellers. The few 'previous rural' (PR) Ansonia residents were excluded from analysis. Three smoking categories were considered: lifetime nonsmokers; ex-smokers of cigarettes; and current cigarette smokers (Table 2).

Questionnaire

We used an extended version of the MRC bronchitis questionnaire (for text, see ref. 4). Questions were prompted by computer and read by trained interviewers; answers were recorded in computer memory. There has thus been no omission or loss of data. Detailed written instruction and supervision of interviewers by the investigators promoted consistency in the interviews. We were unable to allocate subjects at random to interviewers, but an examination of symptom prevalences by interviewer showed that interviewer variation had no important effects on our results. Previous urban (PU) and lifetime rural residents of Lebanon were seen by the same interviewers; interviewer variation can be excluded as a cause of differences between these groups.

Chronic bronchitis

First, we examined the symptom complex of chronic bronchitis (usual cough and phlegm, more than 3 months per year for ⩾ 2 yr). In groups of men and women by age (25+ yr) and smoking habits, smokers always had higher prevalences than nonsmokers or ex-smokers, but urban–rural differences were absent in all groups. For example, 19.0% of the rural male adult current smokers had chronic bronchitis, compared with 17.0% of their urban counterparts. Among both urban and rural residents aged ⩾ 45 yr, the prevalence of chronic bronchitis was less than half that found (with identical methods) among active and retired textile workers at risk from occupational cotton dust exposure[4].

Asthma

A history of bronchial asthma ('yes' to the question 'have you ever had bronchial asthma?') was more common among rural than among urban residents, regardless of age. The difference was highly significant for males (6.7% in 1,142 rural (= LR + PU) males; 2.6% in 458 urban males; $\chi^2 = 9.99$, $P < 0.01$) and similar differences, although not significant, persisted when only lifetime urban and rural residents were compared and when smoking was excluded by comparing only nonsmokers. Smoking habits were not significantly related to a history of bronchial asthma (χ^2 analysis).

Cough, phlegm and other symptoms

Chronic bronchitis may be an insensitive index of urban–rural differences because it is uncommon among nonsmokers. For its component symptoms, as well as wheezing and dyspnoea, we examined the relative importance of the residence variable and of sex, age and smoking habits in a weighted-least-squares analysis[5] of all data in 15–64-yr-old nonsmokers and current smokers. We omitted children, because few of them had any symptoms, and the elderly, because they were too few in number. We also excluded ex-smokers; their symptom prevalences were usually close to those of nonsmokers. Table 3 summarises the best-fitting models. Cigarette smoking was the only variable consistently associated with increased prevalence of all symptoms, at $P < 0.001$. For usual cough and phlegm, a linear residence variable (that is, LU > PU > LR) was highly significant among nonsmokers but not among smokers. The linear residence variable for dyspnoea was complicated by interactions between sex and smoking and between LU residence and smoking. The association between residence and dyspnoea was most pronounced among nonsmoking women (that is, 12.8% in 211 LR compared with 19.2% in 151 LU women). Among nonsmokers (men and women), LR residents had the lowest dyspnoea prevalence, among smoking men and

Table 1 The two towns and their air qualities

	Lebanon (Rural)	Ansonia (Urban)
No. of inhabitants	3,800	21,200
No. of inhabitants per km^2	29	1,178
No. of dwellings per km^2	12	248
No. of vehicles per km^2	26	650
No. of commercial buildings and factories per km^2	0.03	17.8
Sulphur dioxide ($\mu g\,m^{-3}$)	10.9 ± 1.6 (41)	13.5 ± 1.7 (50)
Total suspended particulates ($\mu g\,m^{-3}$)	39.5 ± 4.2 (44)	63.1 ± 3.7 (50)
Nitrogen dioxide ($\mu g\,m^{-3}$)	55.5 ± 6.1 (41)	87.8 ± 4.9 (50)
Ozone ($\mu g\,m^{-3}$)	84.7 ± 4.4 (28)	88.5 ± 3.3 (35)

Demographic and geographical data from 1970 US Census, US Geological Survey maps, and municipal registries. Air pollutant data were obtained at 3–5 sites in Lebanon and at 4 sites in Ansonia, from January to December 1973, and are means ± s.e.m. of 24-h average concentrations, except for ozone values, which are means ± s.e.m. of peak 1-h concentrations (no. of observations in parentheses). Pollutant measurements (for methods and details, see refs 1, 2) were made with supervised, accurately calibrated samplers placed 120 cm above ground level, at least 16 m from any road and at least 11 m from physical obstructions (such as homes, trees). TSP and NO_2 were significantly ($P < 0.001$) higher in Ansonia than in Lebanon, SO_2 and O_3 did not differ significantly.

Table 2 Population groups by sex, age, residence and smoking habits

Residence		Age (yr)					Smoking			Total
Males		7–14	15–24	25–44	45–64	65+	NS	XS	S	
Lifetime rural (LR)		232	116	152	96	18	342	122	150	614
Previous urban (PU)		117	49	135	72	20	165	90	138	393
Lifetime urban (LU)		81	81	71	74	17	144	77	103	324
Previous rural (PR)		2	6	9	10	5	14	9	9	32
	Totals	432	252	367	252	60	665	298	400	1,363
Females										
Lifetime rural (LR)		228	133	195	107	23	456	85	145	686
Previous urban (PU)		112	84	200	95	21	274	78	160	512
Lifetime urban (LU)		101	96	95	136	26	275	59	120	454
Previous rural (PR)		4	6	13	14	4	29	7	5	41
	Totals	445	319	503	352	74	1,034	229	430	1,693

LR, lifetime residence in Lebanon and other rural areas; PU, current Lebanon rural resident but past residence in urban areas; LU and PR, lifetime urban and previous rural residents of Ansonia. Total number of subjects (3,056) represents the total studied (3,387) minus 331 excluded for one or more of three reasons: (1) smokers of pipes or cigars only, (2) 1 yr or longer work in dusty occupations (mines, quarries, foundries, potteries, cotton mills, asbestos factories); (3) unclear history of previous residence (urban or rural). Lifetime nonsmokers (NS) had never smoked tobacco in any form; additional smoking of pipes or cigars by ex-smokers (XS) or current cigarette smokers (S) was not considered. Among children (7–14 yr) the number of ex-smokers and smokers was too small for analysis.

women the PU residents had the highest prevalence (30.8% compared with 21.5% in both LR and LU residents). Residence effects were less significant or absent for wheezing, and they were complicated by interactions with age. The significant age variables in Table 3 reflect higher prevalences among older than younger subjects, except for usual cough, where the 25–44-yr-olds had more symptoms than those who were younger or older. Sex was significant for usual phlegm, being more common among men, and for dyspnoea, which was more prevalent among women.

Figure 1 shows the observed prevalences of usual phlegm in relation to all variables which contribute significantly to its prevalence. There are no interactions, and the fit of the model is the best of all five in Table 3. Observed prevalences among women are similar to those predicted by the model. Among young urban male nonsmokers, the model seems to overpredict prevalence, but the difference between actual and predicted prevalence is not significant. All smokers, regardless of residence, have a higher prevalence of usual phlegm than do LU nonsmokers.

Lung function

We selected the maximum expiratory flow volume (MEFV) curve as a simple, sensitive and comprehensive lung function test[6]. It provides information on lung volume (forced expiratory vital capacity, FVC) as well as maximum expiratory flow rates. In previous studies, maximum flow at mid-vital capacity (MEF 50%) detected airway-constrictor effects of cigarette smoke[7], textile dust[8] and air pollutants[9] better than did measurements such as peak flow or forced expiratory volume in 1 s ($FEV_{1.0}$). We recorded MEFV curves on-line with a computer[10], calibrated every 2 h with a standard curve delivered by a mechanical device[11]. From data on healthy lifetime nonsmokers (by race, sex and age group) in three US communities, including Lebanon and Ansonia, we have derived regression equations for FVC, $FEV_{1.0}$, the $FEV_{1.0}$/FVC ratio, peak expiratory flow rate (PEF) and maximum flow rates at two other points on the MEFV curve (MEF50% and MEF25%), as a function of age, height and weight[12]. In the present study, these equations served to account for effects of age, height and weight in comparisons of lung

Table 3 Weighted least squares analysis of symptom prevalences

Symptom	Variables				Interactions			Fit of model	
	Smoking	Residence	Age	Sex	Age with:	Smoking with:	LU residence with:	P	% Variation explained
Cough	+++	+++*	++	0	Sex +++			0.719	74.8
Phlegm	+++	+++*	+	+++				0.998	81.1
Recent wheeze	+++	+†	+	0	Smoking ++		Age +	0.759	79.7
Frequent wheeze	+++	0	0	0	Residence ++			0.962	67.4
Dyspnoea 1+	+++	+++‡	++	+++		Sex ++	Smoking +++	0.910	77.7

The table includes variables and interactions which contributed significantly to the explanation of the variation in symptom prevalence among all lifetime nonsmokers (NS) and current smokers (S) in Lebanon and Ansonia (age 15–64 yr). Logistic models always gave a better fit than did additive models. If x is the proportion of subjects with symptoms, the logistic model uses a logarithmic transformation of x, that is, $\ln[x/(1-x)]$, as the sum of effects of smoking, residence, age, sex and their interaction. Definition of symptoms: Cough and phlegm on most days for at least 3 months per year; recent wheeze, wheeze within past 12 months; frequent wheeze, wheeze at least a few times each week; dyspnoea 1+, dyspnoea when hurrying on level ground or walking uphill, or worse. Significance of variables and interactions: +++, $P \leq 0.001$; ++, $0.001 < P \leq 0.01$; +, $0.01 < P \leq 0.05$; 0, not significant. Explanation of interactions: Age × sex: difference between sexes (M > F) increases with age. Age × smoking: age increase of prevalence greater for NS than S. Age × residence: 25–64-yr-old PU residents more wheeze than LR and LU; 15–24-yr-olds lower prevalence regardless of residence. Smoking × sex: less effect of smoking in females than males; NS females have relatively high prevalence. LU residence × age: effect of residence on prevalence increase more pronounced in 25–44-yr-olds than in 15–24- and 45–64-yr-olds. LU residence × smoking: LU smokers have lower prevalence than LR and PU smokers; LU nonsmokers have higher prevalence than LR and PU nonsmokers.

* Linear residence variable significant within NS only.

† LR < PU = LU, $P = 0.045$.

‡ Linear residence variable significant for NS and S.

function between groups of subjects. These comparisons were based on calculations of lung function residuals, that is, the differences between observed and predicted values of each measurement.

Analysis of variance of lung function residuals (Fig. 2) among LR, PU and LU residents by sex, age and smoking habits showed no significant differences for any of the measurements. LR, PU and LU nonsmokers had similar residuals, none of which differed significantly from zero or from each other. Smoking adults, on the other hand, had significantly more negative residuals than comparable nonsmokers, regardless of residence. Inclusion of adults with occupational exposure hazards (see legend to Table 1 for definitions) gave results similar to those in the population which excluded these persons.

Susceptible groups

Urban air pollution might not affect all residents, but only unusually sensitive groups within the urban population. Our data suggest that, if such groups exist, they cannot be readily identified on the basis of age (in those aged ≥ 7 yr), sex, race or smoking habits. Attempts to identify susceptible subgroups from questionnaire data were equally unsuccessful. Among smokers, the amount smoked seemed to be the main variable, affecting both symptom prevalence and lung function (unpublished observations); and there were too few nonsmoking urban (LU) residents who reported a history of asthma to allow a comparison of the severity of asthma among urban and rural residents. Among residents with usual cough and phlegm, lung function losses were minimal and not significant either among rural (LR) or urban (LU) residents. Thus, although there may be small groups of persons sensitive to factors in the urban environment that do not affect most people, we have not been able to identify them.

The 'urban factor'

Studies in several US cities[13] have linked excess chronic bronchitis among smokers and nonsmokers to sulphur oxide and particulate pollution. In contrast, we have found that only lesser degrees of certain symptoms, not the composite syndrome of chronic bronchitis, may be associated with urban air pollution, and that this association only occurs in nonsmoking adults (age 15–64 yr; Table 3, Fig. 1). Among smokers, the influence of smoking overrides any differences associated with residence. However, the differences in symptom prevalences between urban and rural nonsmokers are not accompanied by differences in lung function. Even flows on MEFV curves (MEF50%; MEF25%), which are sensitive indices of airway obstruction[14], did not differ. Thus, we have no objective evidence for substantial differences in respiratory health between urban and rural residents.

In the absence of lung function changes, what meaning should be attributed to the higher symptom prevalences among urban and previous urban nonsmokers? They might be due to trivial variables such as a different perception of questions by city and country people. The greater prevalence of dyspnoea among urban (LU) than rural (LR) nonsmoking women might be related to body weight (on average 4.1 kg more in 25–64-yr-old LU women than LR women). However, the LU–PU–LR gradient in prevalence of cough and phlegm among nonsmokers might reflect slight differences in respiratory health. For example, hypersecretion of bronchial mucus (leading to cough and phlegm production) may be more common among urban than rural nonsmokers. This disorder need not lead to progressive lung function loss[15]. It may be part of an adaptive mechanism (for example, increased mucus production may aid the clearance of pollutants) or it might represent incipient illness. Sputum from people in a polluted urban area may contain increased numbers of phagocytes and white cells[16]; these might secrete proteolytic enzymes which damage alveolar tissue[17], or they may protect lung tissue against inhaled particles, or both. No firm conclusion is possible, but the lack of function loss among our older symptomatic, lifetime nonsmoking urbanites suggests that the increased symptom prevalences are not associated with significant long-term deleterious effects on the lungs. Nor does our study indicate additive or synergistic effects between air pollution and smoking: lung function loss among smokers was similarly regardless of residence.

Table 4 Lung function in nonsmoking California and Connecticut residents

	Los Angeles	San Diego	Connecticut		
			LU	PU	LR
O_3 ($\mu g\,m^{-3}$)	~300	~150	~100	~100	~100
TSP ($\mu g\,m^{-3}$)	124	78	65	42	42
No. subjects	90	135	73	41	56
Height (cm)	162	163	158	157	160
$FEV_{1.0}$ (l)	2.44	2.43	2.10	2.08	2.25
MEF50% ($l\,s^{-1}$)	3.38	3.37	2.96	2.81	3.09

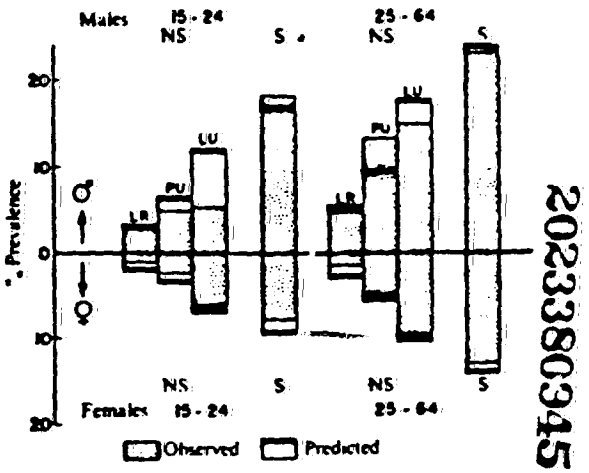
Data for white, female, lifetime nonsmokers aged 45–64 yr. Los Angeles and San Diego data from Cohen *et al*[20]. Data for males are similar. Higher lung function values in nonsmoking California women are explained by their height. All function values are close to those predicted for healthy nonsmoking adult white females[17].

Our study cannot distinguish between air pollution and other urban factors as possible causes of the increased symptom prevalences among PU and LU nonsmokers. However, in a study designed to detect effects of air pollution peaks on daily symptoms among women in high- and low-pollution areas near Rotterdam, Wever[18] found significant associations, mostly in nonsmokers, of pollution peaks with cough, phlegm and dyspnoea, but rarely with wheezing. The similarity of Wever's findings to our own supports the assumption that in Ansonia, too, air pollution may be the 'urban factor' responsible for increased symptoms in lifetime urban nonsmokers.

Expanding the pollution contrast

We have examined the effects of greater air pollution contrasts than existed between Ansonia and Lebanon in three ways: (1) by considering health effects of high indoor pollutant levels in homes, (2) by comparing our findings with those of others, in areas with pollutant concentrations higher than those in Ansonia, (3) by examining respiratory health data from people living in clean rural areas.

Fig. 1 Per cent prevalence of usual phlegm by sex, age, smoking and residence (LR, PU and LU explained in Table 2). Predicted prevalences are those obtained from the model summarised in Table 3. Only significant variables are shown, for example, smokers were not subdivided according to residence as this variable was only significant among nonsmokers.



(1) Suspended particulates indoors are predominantly small-sized (<1 μm diameter) and thus able to penetrate into small bronchi and alveoli[19]. Hence, with equal TSP concentrations, indoor air might be more damaging to health than outdoor air, in which large particles are kept suspended by air currents. However, we found no evidence that the high TSP levels (up to 400 μg m^{-3}) in homes with smokers (ref. 20 and H. R. Hosein *et al.*, unpublished observations) were associated with increased symptoms or lung function loss among nonsmokers in the same

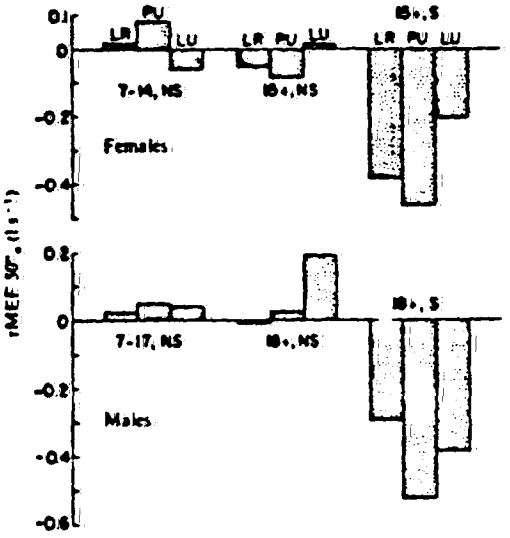


Fig. 2 Mean residual MEF50% (instantaneous maximum flow at 50% FVC) Residual (rMEF50%) = observed − predicted value. None of the differences between residential groups (LR, PU, LU, see Table 2) are significant in any of the six groups by sex, age and smoking habits. For boys and girls, this was also true when a further subdivision was made according to age (7–9 yr, 10–14 yr, 15–17 yr), and differences between LR, PU and LU residents were examined within each of these age and sex groupings. Differences between adult smokers and nonsmokers were significant within each residential subgroup (for example, LR smoking compared with nonsmoking males or females). For purposes of illustration, MEF50% is shown in l s^{-1}. The statistical analyses were, however, done on residuals in transformed units. In MEF50% in children and √MEF50% in adults, these transformations were required to obtain satisfactory prediction equations (see ref. 12 for the equations and their derivation). The equations with transformed units provide residuals which are normally distributed and have equal variances independent of age; height and weight within each subgroup by sex and age group. Values for s.e.m. residuals range over 0.037–0.085 in females and boys, and 0.1113–0.1755 in adult male groups. Differences between mean residuals in smoking groups may reflect differences in amounts smoked; although differences in amounts smoked were not significant between residential groups, PU men and women smoked more than LR and LU men and women.

homes. Nor did we find evidence for loss of lung function among children living in homes with parents who smoked[21]. Thus, much higher TSP concentrations than those which occurred outdoors in Ansonia may still be subthreshold with respect to health effects.

(2) SO_2 and TSP concentrations have previously been high in many urban areas. In the UK, very high pollution levels (up to 1,160 μg m^{-3} SO_2) which occurred in 1965 and previous years, were clearly associated with exacerbations of bronchitis[22]. However, pollution levels lower than those in the UK in the 1950s and early 1960s do not seem to have any marked effect on health. For example, results similar to ours (a slight excess of cough and phlegm) were obtained among men employed in Manhattan in 1962–63 (ref. 23), before current air pollution control programmes began, and at a time when SO_2 and TSP were of the order of 500 μg m^{-3} and 250 μg m^{-3}, respectively[19]. At about the same time (1961–62), nonsmoking black and white male postal or transit workers in New York City[24,25] had $FEV_{1.0}$ values almost identical to those in our urban and rural nonsmokers in 1973 when age, race and height are taken into account. According to our equations describing growth of lung function in children[12], Czech children (age 10–11 yr) living in a town with high SO_2 (annual mean 150–170 μg m^{-3})[26] and TSP (annual mean 100–110 μg m^{-3})[26] concentrations have lung function values[27] very close to those of 10–11-yr-old children in Ansonia and Lebanon.

Oxidant pollution has not been clearly linked with increased prevalence of chronic bronchitis or its component symptoms; in fact, chronic bronchitis seems to be about as uncommon among Los Angeles nonsmokers[28] as among our rural (LR + PU) nonsmokers of the same age (45–64 yr), that is, 1.7 and 1.5%, respectively. Nonsmokers in Los Angeles, exposed to higher oxidant and TSP concentrations, and nonsmokers in Connecticut have similar lung function when height is taken into account (Table 4).

(3) The lack of important contrasts in air pollution and respiratory health between Ansonia and Lebanon might be explained if Lebanon were a relatively polluted rural area. However, we have found no evidence that respiratory health is demonstrably better in pristine rural areas. Nonsmokers in such an area (Chilliwack, British Columbia) had higher prevalences of cough and phlegm[29] than our lifetime urban nonsmokers. Residents of Winnsboro, South Carolina (with significantly lower SO_2 and NO_2 concentrations than those of Lebanon[1]) had symptom prevalences and lung function similar to those of Lebanon residents, and a higher prevalence of a history of asthma (unpublished observations). Black children and adults in a primitive village in Upper Volta, away from cities and with minimal automotive traffic[30], had FVC and $FEV_{1.0}$ values similar to those we recorded among urban black residents in Ansonia and rural black residents in South Carolina.

We conclude from these comparisons between our data and those of others that even relatively low levels of air pollution (as in Ansonia) may be associated with a slight excess of some respiratory symptoms in nonsmokers, but that these symptoms may only become noticeably worse when SO_2 and particulates reach levels higher than those prevailing in Manhattan in 1962–63. Even high concentrations of SO_2, TSP and oxidants by current US standards are not associated with loss of lung function when sex, race, age, height and weight are adequately taken into account.

Implications

The overall impact of outdoor air pollution on respiratory health in Ansonia residents seems to be minimal. Even though the levels of air pollution in Ansonia are low by the standards of the UK in the 1950s, this is of interest because Connecticut is frequently said to have "the worst air pollution in the country outside Los Angeles" (ref. 31). However, any effect of air pollution in Ansonia is small compared with the effects of cigarette smoking and of certain occupational exposure hazards, such as occur among cotton textile workers[4]. Nor have we found evidence that outdoor air pollution worse than that in Ansonia (for example, in Los Angeles[28], New York[23,24,25], Rotterdam[18] or Czechoslovakia[26,27]) produces substantially greater effects on health. Our conclusions are valid for those lung disorders which affect vital capacity and air flow rates; these include asthma, bronchitis and emphysema. There may be sensitive subgroups within the general population which we have not been able to detect, but this remains speculation.

The extent to which communities want to abate air pollution, and the economical burdens which they are willing to accept for that purpose, are matters for society to decide. There are many reasons, aesthetic as well as hygiene-related, for reducing urban air pollution. Within rather wide margins, however, variations in air quality do not seem to have substantial effects on the

prevalence and severity of common diseases which affect airway calibre.

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Molecular structure of a double helical DNA fragment intercalator complex between deoxy CpG and a terpyridine platinum compound

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The crystal structure of a complex containing deoxy CpG and a terpyridine platinum compound (TPH) shows a DNA double helical fragment with TPH intercalated between two Watson–Crick GC base pairs. The DNA unwinding angle is 23° and the pucker of the deoxyribose rings differ at the 3' and 5' ends.

STUDY of the molecular structure of nucleic acid components is of considerable interest in developing an understanding of the macromolecular nucleic acids. Single crystal X-ray diffraction analysis allows us to determine unambiguously several geometrical details concerning these molecules. Studies from this laboratory[1–4] showed that it was possible to crystallise self-complementary ribodinucleoside phosphates as double helical fragments with Watson–Crick hydrogen bonding between the bases. An interesting application of these studies is their extension to double helical fragments which crystallise with planar molecules intercalated between their base pairs. Lerman[5] postulated that certain classes of planar molecules, many of which are mutagenic or carcinogenic, act by insertion between adjacent base pairs in the DNA double helix. Several structural studies have supported this interpretation. Sobell and his colleagues[6,7] described the structure of an RNA double helical fragment which contained an intercalator and several different structures of this type have now been solved with a variety of intercalators lodged inside double helical ribonucleotide fragments[8–11]. These crystallographic studies show that the pucker of the ribose ring is modified by the insertion of an intercalator between the base pairs. However, a major difference between DNA and RNA double helices is the different pucker of the sugar ring. It is therefore of interest to ask how intercalation will modify the geometry of the DNA backbone especially with regard to the pucker of the deoxyribose ring[12].

In this article we report the crystal structure of a complex containing deoxycytidylyl-(3',5')-deoxyguanosine (deoxy CpG) which has crystallised with the intercalator 2-hydroxyethanethiolato-2,2',2''-terpyridine-platinum (II) [TPH][13,14]. In this structure, deoxy CpG forms an antiparallel double helix in which the helix has unwound and the base pairs are unstacked with one TPH molecule intercalated between the base pairs of the double helical fragment. Another TPH molecule is stacked between double helical fragments in the lattice. This structure allows us to determine directly both the unwinding angle of the DNA double helical fragment as well as the pucker of the deoxyribose rings.

Experimental methods

The dimer deoxy CpG was prepared using the phosphotriester method[15,16]. The dimer thus obtained was converted into the ammonium salt by passing it twice over a Dowex cation-exchange resin in the NH_4^+ form. The material was freeze dried

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